PRISM study: Comparison of a nystatin-neomycin-polymyxin B combination with miconazole for the empirical treatment of infectious vaginitis

Abstract

Objective. – An empirical treatment of infectious vaginitis is justified because of its multiple etiologies, the frequent uncertainty of clinical diagnosis and limits of microbiological analysis. Our aim was to comparatively investigate nystatin-neomycin-polymyxin B combination (NNP, Polygynax®) and miconazole.

Patients and methods. – In this European multicenter, double-blind PRISM trial, participating women presenting with infectious vaginitis were randomized to receive one vaginal capsule containing either NNP for 12 days or miconazole for 3 days followed by 9 days of placebo.

Results. – The clinical success rate was higher in the NNP group (n = 302) than the miconazole group (n = 309), with a difference between groups close to statistical significance (91.1% vs. 86.7%, \( P = 0.0006 \)). The risk of treatment failure was 36% lower in the NNP group (odds ratio, 0.64; 95% confidence interval, 0.38–1.07). Vaginal burning on Day 2 and vaginal discharge on Day 4 were significantly less intense in the NNP group than in the miconazole group (39.1% vs. 42.3, \( P = 0.031 \) and 34.6% vs. 37.6, \( P = 0.031 \), respectively). Adverse drug reactions were reported by 1.2% and 2.1% of patients in the NNP and miconazole group respectively, with the ratio of adverse drug reactions relative to total adverse events significantly higher in the miconazole group (20.3% vs. 6.9%, \( P = 0.02 \)).

Conclusion. – The widespread use of NNP for several decades and its good efficacy and safety profile, as well as the frequent diagnostic uncertainties due to the various pathogens sustain the initiation of this broad-spectrum empirical treatment in infectious vaginitis.

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Keywords : Bacterial vaginitis ; Nystatin ; Neomycin ; Polymyxin B ; Vaginal yeast infection

Résumé

Objectif. – Le traitement probabiliste de la vaginite infectieuse se justifie par sa diversité étiologique et l’incertitude fréquente du diagnostic clinique et microbiologique. L’objectif était de comparer l’association nystatine-néomycine-polymyxine B (NNP) au miconazole.

Patients et méthodes. – Dans cet essai multicentrique européen en double insu, les participantes présentant une vaginite infectieuse ont été randomisées pour recevoir par voie vaginale le NNP pendant 12 jours ou le miconazole pendant 3 jours puis un placebo pendant 9 jours.


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1. Introduction

Vaginitis is a common condition characterized by an increased vaginal discharge with abnormal consistency, color, or odor [1]. Vaginitis has an infectious origin in 90% of cases [2]. Three common types of vaginal infections are reported: bacterial vaginosis related to a change in the normal lactobacilli flora (vaginal dysbiosis), vulvovaginal candidiasis due to yeasts, and trichomoniasis which is a sexually-transmitted infection [1]. In contrast to vaginitis, there is no local inflammation in vaginositis [3].

Besides this typical triad, other clinical entities are now recognized to account for a significant percentage of infectious vaginitis:

* bacterial vaginitis, mainly caused by enteric bacteria such as *E. coli*, unlike bacterial vaginosis where anaerobic bacteria (e.g., *Gardnerella vaginalis*) are predominant [3];
* mixed vaginitis due to at least two vaginal pathogens that both contribute to the clinical picture of vaginitis [4].

The microbiological etiologies of infectious vaginitis reported in a recent French study of 169 women presenting with vaginitis were as follows:

* vulvovaginal candidiasis (55.1%);
* mixed vaginitis (32.2%);
* bacterial vaginosis (7.6%);
* bacterial vaginitis (5.1%) [5].

Microscopic evaluation of vaginal fluid is recommended in women presenting with vaginitis [1]. Microbial culture is also used but false negative and positive results are frequent depending on the sampling site, the phase of the menstrual cycle, or asymptomatic carriage [6–8]. Furthermore, the limitations of this traditional approach have been stressed with the development of metagenomic diagnostic techniques [9,10]. Pending their routine use, an empirical treatment is therefore justified for immediate care while awaiting microbial results. Although antifungals (azoles) are frequently prescribed in case of typical signs and symptoms of vulvovaginal mycosis [11], a broad-spectrum local treatment is preferably initiated as first-line therapy in other situations for fast and effective relief of symptoms. Polygynax® is a local treatment that combines two antibiotics, neomycin and polymyxin B, and one antifungal, nystatin (NNP). Neomycin is a broad-spectrum antibiotic active against Gram-negative and some Gram-positive bacteria; polymyxin B is a polypeptide antibiotic with antimicrobial activity restricted to Gram-negative bacteria; and nystatin is a polynye antifungal agent used in the local treatment of yeast infections. The NNP combination within a vaginal capsule covers the majority of pathogens involved in infectious vaginitis [12–14].

This NNP combination has been marketed since 1969 and is widely used in this indication. However, comparison of efficacy and safety in current clinical practice over other local treatments of infectious vaginitis is lacking [14]. We designed a randomized, double-blind, comparative trial to compare NNP with miconazole in the empirical treatment of infectious vaginitis (excluding sexually-transmitted infections).

2. Patients and methods

2.1. Type of study

The Polygynax® as EmpiRical Treatment of Infectious VaginitiS: AssessMent of the Efficacy study (PRISM) was an international, multicenter, randomized, double-blind, parallel-group, comparative phase IIIb study. Patients from four countries (France, Serbia, Czech Republic, Slovakia) were included by gynecologists and family physicians with strong knowledge of gynecology.

The objective of the PRISM study was to demonstrate the superior clinical efficacy of NNP compared with miconazole in the empirical treatment of infectious vaginitis. Safety, compliance, and global satisfaction of patients and investigators were also assessed.

Written informed consent was obtained from each patient. The protocol was conducted in accordance with the Declaration of Helsinki and Good Clinical Practices and was approved by local independent Ethics Committees. This study is registered with the ClinicalTrials.gov identifier NCT02515656.

2.2. Population included

Outpatient women aged 18–64 years and able to receive empirical local treatment were included if they had abnormal
vaginal discharge associated with at least one functional vaginal complaint (burning, pain, or irritation) suggesting infectious vaginitis such as bacterial vaginitis, non-specific vaginitis (atypical symptoms), or mixed vaginitis (i.e., superinfected fungal vaginitis) at clinical examination. The main exclusion criteria were:

- recurrent infectious vaginitis (i.e., at least four episodes within 12 months);
- vaginal infection eligible for systemic therapy;
- history or suspicion of atrophic vaginitis;
- clinical signs of genital herpes or non-infectious vulvar pathology (vulvodynia, psoriasis, eczema, lichen sclerosus, lichen planus, contact dermatitis, Candida intertrigo, vulvar intraepithelial neoplasia);
- or non-infectious vulvar pathology (vulvodynia, psoriasis, eczema, lichen sclerosus, lichen planus, contact dermatitis, Candida intertrigo, vulvar intraepithelial neoplasia);
- presence or clinical suspicion of sexually-transmitted infection (STI);
- disease or concomitant treatment possibly associated with immunodeficiency (i.e., diabetes mellitus, corticosteroids);
- systemic antimicrobial treatment (antibiotic, antifungal) within two weeks;
- menstrual periods or menometrorrhagia due to hormonal imbalance;
Table 1
Characteristics of patients at inclusion (FAS population, as treated).
Caractéristiques des patientes à l’inclusion (population FAS, conformément au traitement reçu).

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>NNP (n = 302)</th>
<th>Miconazole (n = 309)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Age (years), mean (SD)</em></td>
<td>34.7 (10.1)</td>
<td>33.7 (10.1)</td>
</tr>
<tr>
<td>Body mass index (kg/m²), mean (SD)</td>
<td>23.3 (4.1)</td>
<td>23.3 (4.7)</td>
</tr>
<tr>
<td><em>Post-menopausal women, n (℅)</em></td>
<td>18 (6.0)</td>
<td>14 (4.5)</td>
</tr>
<tr>
<td>Vaginal infection within one year, n (℅)</td>
<td>90 (29.8)</td>
<td>99 (32.0)</td>
</tr>
<tr>
<td>Previous treatment for current vaginal infection, n (℅)</td>
<td>11 (3.6)</td>
<td>5 (1.6)</td>
</tr>
<tr>
<td><strong>Functional vaginal complaints, n (℅)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burning and irritation</td>
<td>92 (30.5)</td>
<td>99 (32.0)</td>
</tr>
<tr>
<td>Burning, pain, and irritation</td>
<td>89 (29.5)</td>
<td>92 (29.8)</td>
</tr>
<tr>
<td>Irritation</td>
<td>53 (17.5)</td>
<td>57 (18.4)</td>
</tr>
<tr>
<td>Burning</td>
<td>37 (12.3)</td>
<td>33 (10.7)</td>
</tr>
<tr>
<td>Pain and irritation</td>
<td>12 (4.0)</td>
<td>11 (3.6)</td>
</tr>
<tr>
<td>Burning and pain</td>
<td>12 (4.0)</td>
<td>8 (2.6)</td>
</tr>
<tr>
<td>Pain</td>
<td>7 (2.3)</td>
<td>9 (2.9)</td>
</tr>
<tr>
<td><strong>Leukorrhea score</strong></td>
<td></td>
<td></td>
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<tr>
<td>Absent</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mild</td>
<td>35 (11.6)</td>
<td>38 (12.3)</td>
</tr>
<tr>
<td>Moderate</td>
<td>189 (62.6)</td>
<td>197 (63.8)</td>
</tr>
<tr>
<td>Abundant</td>
<td>78 (25.8)</td>
<td>74 (23.9)</td>
</tr>
<tr>
<td><strong>Intensity (VAS) of vaginal symptoms (mm), mean (SD)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discharge</td>
<td>55.2 (22.4)</td>
<td>54.7 (22.6)</td>
</tr>
<tr>
<td>Burning</td>
<td>45.7 (28.9)</td>
<td>43.8 (28.3)</td>
</tr>
<tr>
<td>Pain</td>
<td>31.5 (26.9)</td>
<td>30.0 (26.5)</td>
</tr>
<tr>
<td>Irritation</td>
<td>47.3 (27.4)</td>
<td>46.5 (26.4)</td>
</tr>
<tr>
<td><strong>Type of vaginitis suspected (clinical examination)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacterial vaginitis</td>
<td>58 (19.2)</td>
<td>58 (18.8)</td>
</tr>
<tr>
<td>Vaginitis with atypical symptoms</td>
<td>74 (24.5)</td>
<td>73 (23.6)</td>
</tr>
<tr>
<td>Mixed vaginitis</td>
<td>170 (56.3)</td>
<td>178 (57.6)</td>
</tr>
<tr>
<td><strong>Results of the microbiological examination at inclusion, n (℅)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No detected infection</td>
<td>87 (28.8)</td>
<td>78 (25.2)</td>
</tr>
<tr>
<td><em>Candida</em> vaginitis</td>
<td>72 (23.8)</td>
<td>75 (24.3)</td>
</tr>
<tr>
<td>Mixed vaginitis</td>
<td>57 (18.9)</td>
<td>53 (17.2)</td>
</tr>
<tr>
<td>Bacterial vaginitis</td>
<td>41 (13.6)</td>
<td>40 (12.9)</td>
</tr>
<tr>
<td>Bacterial vaginosis</td>
<td>28 (9.3)</td>
<td>46 (14.9)</td>
</tr>
<tr>
<td>Imbalance of vaginal flora alone</td>
<td>17 (5.6)</td>
<td>17 (5.5)</td>
</tr>
</tbody>
</table>

FAS: full analysis set; NNP: nystatin, neomycin, and polymyxin B; SD: standard deviation; VAS: visual analogue scale.

- pregnancy;
- breastfeeding;
- or delivery within one month

2.3. Study procedures

A gynecological evaluation was performed by the investigator during three scheduled visits: baseline visit (Day 1), end-of-treatment visit (Day 15), and end-of-study visit (Day 22). The leukorrhea was quantified by the investigator using a specific score (absent; mild: insufficient for speculum collection; moderate: sufficient for speculum collection; abundant: visible at the vaginal introitus before speculum introduction).

Patients were asked to assess each vaginal symptom (discharge, burning, pain, irritation) for 14 days using a visual analogue scale (VAS) and recorded the results in a diary.

A vaginal sample was obtained from each patient during per speculum examination at inclusion. Vaginal samples were analyzed in a microbiology laboratory (one centralized laboratory in each country). Direct microscopic examination (Nugent score and search for blastospores and mycelial filaments), mycobacteriological examination (inoculation on different enriched agar media), and assessment of STI (*Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis*) by nucleic acid amplification test were performed. Results of microbiological analyses were transmitted to the investigator during the study only in case of STI.

Both the investigator and the patient completed a 6-point scale global satisfaction questionnaire related to the study treatment (very good, good, somewhat good, somewhat bad, bad, very bad) on Day 15.

Adverse events spontaneously reported by patients or observed by investigators were recorded in the case report form. Adverse events were defined as any undesirable medical event occurring at any time during the clinical study, irrespective of its relation to the study treatment. Adverse drug reactions were adverse events judged by the investigator as having a reasonable causal relationship with the study treatment.

2.4. Study drugs

According to the randomization procedure, patients either received a combination of nystatin 100,000 IU, neomycin
sulfate 35,000 IU, and polymyxin B sulfate 35,000 IU (NNP, Polygy-nax®), administered as one intravaginal capsule per day at bedtime for 12 days, or miconazole (Gy-no-Daktarin®), one intravaginal capsule per day administered at bedtime for three days followed by nine placebo vaginal soft capsules. Active and placebo vaginal capsules were identical and presented in the same packaging to ensure blinding of the medication.

2.5. Statistical analysis

The sample size was based on expected success rates equal to 78% in the comparator group and 88% in the NNP group. With a 5% two-sided type-one error and a 90% statistical power, we calculated that a difference between groups ≥10% could be evidenced with 294 evaluable patients in each group. Finally, we planned to randomize 650 patients considering 10% of non-eligible or not assessable patients for the primary criterion (including patients presenting with STI).

The full analysis set (FAS) included all randomized patients who received at least one dose of the study medication. Patients presenting with a STI detected from the vaginal sample taken before randomization at baseline visit and patients without post-randomization data were excluded from the FAS. Patients were analyzed according to the treatment they actually received (as treated).

The per protocol set (PPS) included all patients of the FAS without any major protocol deviation. The modified PPS (mPPS) included all patients of the FAS without any major protocol deviation except study treatment not dispensed according to the randomization procedure. The safety set included all enrolled patients who were administered at least one vaginal capsule of the study drug.

Clinical treatment efficacy was assessed by the investigator after thorough gynecological examination and patient interview at end-of-treatment visit (15 days after first treatment administration or after early study discontinuation). Success was defined by resolution (return to the patient’s usual gynecological conditions) or substantial improvement of clinical signs of infectious vaginitis (i.e., abnormal vaginal discharge) and/or vaginal symptoms (burning, pain, irritation). Failure was defined by persistence or worsening of symptoms and clinical signs, or requirement of an alternative or specific treatment. The need to initiate a specific treatment because of a STI detected from the vaginal sample at inclusion visit or patients presenting with only vulvar complaints not considered as related to infectious vaginitis, were not considered failures.

All P-values were two-sided with $P < 0.05$ considered statistically significant.

3. Results

3.1. Patient disposition and characteristics at inclusion

From September 2015 to August 2016, 661 women were enrolled in 66 centers located in four countries (France, Serbia, Czech Republic, Slovakia). A total of 658 patients were randomized to receive either NNP ($n = 326$) or miconazole ($n = 332$) (Fig. 1). The study was completed by 531 patients. Treatment failure ($n = 64$) and STIs ($n = 43$) were the main reasons for early discontinuation ($n = 127$).

Patients’ characteristics are displayed in Table 1. The FAS included 302 patients in the NNP group and 309 patients in the miconazole group, with comparable mean age (34.7 years and 33.7 years, respectively). Other characteristics (body mass index, post-menopausal women, history of vaginal infections) were also comparable, as was the intensity of the various vaginal symptoms. The leukorrhea score was mainly moderate (63.2%) and the most frequent vaginal complaints were vaginal irritation (82.7%) and vaginal burning (75.6%). The most frequent types of infectious vaginitis were *Candida vaginitis* (24.1%) and mixed vaginitis (18.0%) followed by bacterial vaginitis (13.3%) and bacterial vaginosis (12.1%) with comparable percentages between groups. No infection was detected by microbiological examination in 27% of women.

3.2. Efficacy

Overall, 99.3% of patients in FAS were assessable for the primary endpoint, i.e. treatment efficacy (non-assessable patients were considered as treatment failures for the primary endpoint). Success was more frequently observed in the NNP group than in the miconazole group with a difference between groups close to statistical significance (91.1% vs. 86.7%, $P = 0.0906$) (Table 2). This result was confirmed in the PPS and mPPS analyses. Overall, the risk of therapeutic failure was reduced by 36% for patients treated with NNP compared with miconazole, although statistical significance was not achieved (OR, 0.64; 95% CI, 0.38–1.07) (Fig. 2).

Repeated measures of Anova were performed to study the intensity of vaginal symptoms over time (vaginal discharge, burning, pain, and irritation). Mean VAS for all symptoms significantly decreased until Day 14 in both groups ($P < 0.001$ for each symptom). However, the decrease in the scores of vaginal burning on Day 2 and of vaginal discharge on Day 4 was significantly more important with NNP than with miconazole (respectively $-6.2$ vs. $-1.5$, $P = 0.031$ – Fig. 3; and $-20.6$ vs.

<table>
<thead>
<tr>
<th>Table 2</th>
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<tbody>
<tr>
<td>Analysis of the primary efficacy endpoint (FAS, PPS, and mPPS, as treated).</td>
</tr>
<tr>
<td>Analyse du critère principal d’efficacité (populations FAS, PPS et mPPS, conformément au traitement reçu).</td>
</tr>
<tr>
<td>Characteristics $n$ (%)</td>
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<tr>
<td>FAS population (primary analysis)</td>
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<tr>
<td>Assessable primary endpoint</td>
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<tr>
<td>Success</td>
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<tr>
<td>PPS population</td>
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<td>Assessable primary endpoint</td>
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<tr>
<td>Success</td>
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<tr>
<td>mPPS population</td>
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<tr>
<td>Assessable primary endpoint</td>
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<tr>
<td>Success</td>
</tr>
</tbody>
</table>

NNP: nystatin, neomycin, polymyxin B combination; FAS: full analysis set; PPS: per protocol set; mPPS: modified per protocol set.
3.3. Safety

Exposure to the study drug was comparable in both groups. The mean ± SD duration of exposure was 11.9 ± 1.1 days in the NNP group and 11.8 ± 1.1 days in the miconazole group; 96.6% and 95.3% of patients received 12 capsules as planned over the 12-day period, respectively.

Adverse events (AEs) were uncommon in both groups (72 in NNP and 64 in miconazole) and predominantly of mild and moderate intensity. Overall, 44 in the NNP group and 38 in the miconazole group experienced at least one AE (Table 3). The number of adverse drug reactions (ADRs) – AEs considered related to the study drug – was lower in the NNP group (five AEs reported by four patients, 1.2%) than in the miconazole group (13 AEs reported by seven patients, 2.1%). The most frequently reported ADRs, according to the MedDRA System Organ Class classification, were reproductive system and breast disorders (e.g., vaginal discharge, bleeding, pain, pruritus, or burning sensation) [eight (1.2%) patients: two in the NNP group, six in the miconazole group], followed by skin and subcutaneous tissue disorders (pruritus, eczema) [three (0.4%) patients: one in the NNP group, two in the miconazole group], gastrointestinal disorders (abdominal pain) [two (0.3%) patients: one in each group], and general disorders and administration site conditions (pain) in one patient of the miconazole group. There was no significant difference between groups except that the incidence of ADRs relative to the number of AEs (ADRs/AEs) was significantly higher in the miconazole group (20.3%, 13/64) than in the NNP group (6.9%, 5/72, P = 0.022).

One serious adverse event of exposure during pregnancy (pregnancy test negative at inclusion) was reported in the NNP group without any adverse consequence for the mother and the newborn.

Treatment was permanently discontinued due to adverse events in five patients (one in the NNP group and four in the miconazole group).

4. Discussion

The PRISM trial is the first randomized double-blind study that compared nystatin-neomycin-polyoxymyxin B combination (NNP, Polygynax®) with an azole compound (miconazole, Gyno-Daktarin®), both widely used for decades as local treatments of infectious vaginitis. Carried out according to modern standards, this study confirms the high efficacy of NNP marketed since 1969 and supports its well-known safety profile.
Clinical success was numerically more frequent with NNP than with the comparator (91.1% vs. 86.7%, respectively; \( P = 0.0906 \)). This result is consistent with previous multicenter studies, which reported clinical success rates for NNP ranging from 92.2% to 97.8% in the empirical treatment of infectious vaginitis [12,13]. Furthermore, exploratory analyses revealed that vaginal burning and vaginal discharge assessed with visual analogue scales were improved at significantly earlier times with NNP than miconazole. The rapid relief of symptoms being essential in the treatment of infectious vaginitis, these results therefore suggest that future studies on treatments of infectious vaginitis should focus on the early relief of symptoms as primary endpoint and not only on the end-of-treatment scores. This endpoint could be more appropriate for discriminating between local vaginitis treatments that achieve high levels of success.

The distribution of infectious vaginitis according to etiology at inclusion confirms the high percentage of infectious vaginitis other than pure Candida vaginitis reported in previous studies [5,15]. Indeed, pure Candida vaginitis represented 24.1%, followed by mixed vaginitis (18.0%), bacterial vaginitis (13.3%), and bacterial vaginosis (12.1%). Moreover, imbalance of vaginal flora alone was reported in 5.6% of cases. The microbiological examination failed to find any infection in more than 25% of women despite the presence of a typical clinical picture of infectious vaginitis. This rate of non-diagnosis compares favorably with that reported in the medical literature: about one-quarter to one-third of women did not demonstrate laboratory evidence of infection despite the presence of clinical symptoms [6,13,16]. Given that microbiological cultures were examined by experienced personnel, the most likely explanation is that vaginitis symptoms may have resulted from a non-infectious process in some patients. Another explanation could be that some infectious pathogens were not able to grow, and thus to be identified according to the conventional laboratory procedures. It confirms the accuracy limitations of the microbiological diagnosis of vaginitis.

No conclusion concerning the change in microbiological status from baseline to the end of study (ancillary endpoint) can be drawn because of the low number of vaginal samples taken at the end of the study. However, according to the clinical evaluation, similar efficacy levels were obtained with NNP on the various types of infectious vaginitis: Candida vaginitis (94.4%), bacterial vaginitis (85.4%), mixed vaginitis (87.7%), and bacterial vaginosis (96.4%).

The results of this study should be interpreted taking into consideration the context of the clinical routine management of infectious vaginitis. The clinical picture is theoretically supposed to guide the etiological diagnosis of vaginitis and consequently to help in choosing the appropriate treatment. The reality is, however, more complex, particularly in cases of mixed vaginitis, previous self-medication, or local washing just before consultation. Microbiological analysis therefore seems to be essential in identifying the pathogen(s) responsible for the infection. However, due to economic reasons or a lack of adequate facilities or for medical reasons, it is not always possible to do so. Thus, in nearly half of vaginitis consultations, a vaginal swab is not performed. Moreover, the reliability of microbiological examinations (sensitivity and specificity) is now questioned [16–20]. Cultures of the vaginal secretions may also evidence a large variety of pathogens that are not necessarily related to the clinical symptoms, but that are making the interpretation very difficult. Thus, an empirical treatment is commonly initiated in the absence or pending microbiological examination. Moreover, a recent clinical study reported no difference in terms of efficacy outcomes between a treatment of infectious vaginitis guided by microbiological analysis or an empirical medical care [21].

Physicians often choose local azole treatment as first-line treatment as they usually consider unusual leukorrhea or vulvovaginal pruritus as resulting from a Candida spp. infection, known to be the commonest etiology of vaginitis. The azole derivatives are active against mucocutaneous mycosis pathogens (dermatophytes, Candida, and other yeasts) and also against some Gram-positive bacteria. However, as reported in the PRISM study and in a previous study, up to one in five vaginitis cases is mixed and a significant percentage of vaginitis cases are bacterial [5]. In another French study, Candida vulvovaginitis cases were adequately identified and treated by physicians but, for the other infectious vaginitis cases, treatment reassessment was often required [22]. Therefore, the diversity of pathogens justifies a broad-spectrum treatment including antifungal and antibiotic agents active against yeasts, Gram-positive and Gram-negative bacteria.

5. Conclusion

The frequent diagnostic uncertainties due to the various pathogens, the infrequent microbiological examinations or the delays when performed, and the need for rapid symptom relief sustain the initiation of a broad-spectrum treatment in infectious vaginitis. Further investigations with NNP, for instance to explore its potential in the prevention of relapses and recurrences, should strengthen the interest of this combination in the treatment strategy of this common gynecological infection.

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Contribution of authors

J. M. Bobbot was the main investigator of the study.
Y. Mas and F. Verrière provided guidance and advice in the study design and methodology.
A. Goubard was involved in the analysis of microbiological data.
F. Aubard was the statistical expert.
E. Coantaniec and N. Lucas were involved in the management of the study.
Disclosure of interests

J. M. Bohbot, A. Goubard and F. Aubin: scientific consultants for Laboratoire Innootech International.


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Références


